Inflammation
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Inflammation is a cellular response to an injury or abnormal stimulus caused by a physical chemical or biological substance and represents a major component of the human innate response to microbial pathogens.

Pathogen invasion in the gut elicits expression of a range of inflammatory mediators including MCP-1, IL-8, Gro, histamine, IL-1 β. This induction of expression of proinflammatory molecules is mediated through bacterial lipopolysaccharide or its N'terminal-fMet-Leu-Leu- peptides and leads to activation of NF-κB which in turn induces the release of TNF-□ and evokes numerous responses from immune cells and surrounding tissues. Although in general the secretion of TNF-□ is beneficial for rapid activation of immune responses, the prolonged activation of this cytokine favors pathological effects leading to destruction of intestinal epithelium, fluid loss, increased diarrhea and degradation of the structural defenses of the gut.

Different components of bacterial antigens induce inappropriate activation of NF-κB in infected tissues. For example LPS plays a major role during infection by *Shigella flexneri*, *Yersinia enterocolytica Salmonella enterica* and *Shigella dysenteriae.* However, additionally to LPS mediated activation, some strains employ also their toxins to induce NF-□B/DNA binding, as was found for invasin in *Yersinia enterocolytica* or factors of the Type III Secretion System and SipB in *Salmonella enterica* Typhimurium infections. Also the Shiga toxin of *Shigella dysenteriae* Type 1 mediates the expression of TNF-α through inappropriate NF-□B activation.

Currently available therapies are directed to eradication of pathogens, resulting in cessation of virulence factor expression, and concomitant decline in the expression of inflammation factors. However new approaches are needed to target pathogens through improving the host cellular responses to the invasion and making the target cells unavailable for infection. The HIV-1 Resistance Factor (HRF) is a protein expressed by CD4+ T cells that have been induced to resist viral infection. However, we found that exposure to soluble products of HRF-producing cell line impeded NF-□B/DNA binding in human macrophages induced by LPS from several species of bacteria including *Vibrio cholerae, Salmonella minnesota*, and *E. coli* and resulted in impaired TNF-□ responses to these organisms suggesting that HRF might have a broad activity against organisms whose pathogenesis is linked to NF-□B activation.

Subsequent studies on the mechanism of HRF-mediated inhibition of NF-□B/DNA binding showed that HRF interacts with p50 component of NF-□B dimer after it enters to the nucleus, but before its binding to cognate DNA motif and that this interaction impedes the formation of an NF-□B-DNA complex required for the promotion of transcription.

Taking altogether HRF is a novel NF-κB antagonist, a human protein secreted by CD4+ T-cells and offers some promise as a broad spectrum immunotherapeutic to interrupt the inflammatory pathway associated with infection by several different pathogens such as *Salmonella, Shigella, Campylobacter,* and HIV-1.